REMARKS

Applicants have reviewed the Office Action mailed on October 20, 2004 and offer the following remarks. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Election/Restriction

Applicants confirm that claims 1-7 are under consideration. Claims 17-21 is sought to be added. Therefore, Claims 1-7 and 17 -21 are currently pending.

Drawings

Applicants also confirm that the Examiner has accepted the drawings filed on September 25, 2003 on page one (1) of the Office Action.

Priority Under 35 U.S.C. 119(e)

Applicants thank the Examiner for confirmation of the claim for domestic priority for the present application.

Sequence Listing

Applicants acknowledge the corrections to the paper copy and computer readable form of the Sequence Listing filed September 25, 2003 as noted by the Examiner.

Title

The title was objected to by the Examiner. The Applicants have amended the title as suggested by the Examiner.

Claim Objection

An amendment to claim 2 has been made according to the suggestion of the Examiner. It is believed that the concerns of the Examiner have therefore been overcome and the Applicants request that the objection be withdrawn.

Rejection Under 35 U.S.C. § 101

The Examiner has rejected claims 1-9 under 35 U.S.C. § 101. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules lack a specific and substantial asserted utility or a well-established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

The Examiner states that "[b]ased on computer programs that search databases for similarities to the disclosed nucleotide and amino acid sequences, the specification assigns the protein having the deduced amino acid sequence of SEQ ID NO: 2 as a protein that is a member of "drug-metabolizing enzyme family of proteins" and is related to the cytochrome p450 (CYP) drug-metabolizing enzyme subfamily (see specification p. 9, lines 10-13)." The Examiner continues that "Figures 2C of the disclosure shows that Blast computer searches in the databases detected only a 50% identity between SEQ ID NO: 2 and the amino acid sequence of a rabbit cytochrome p450."

The Examiner asserts that "[t]he specification does not disclose any enzyme assays that demonstrate that the protein having the deduced amino acid sequence of SEQ ID NO: 2 has cytochrome p450 activity. The specification does not disclose a specific biological function of the protein having the deduced amino acid sequence of SEQ ID NO: 2." The Examiner additionally states that the specification does not disclose a reference protein known in the art that "the claimed protein *automatically* has the properties and biological function of the reference protein relied on." [emphasis added by Applicants] The Examiner further asserts that the identification of the claimed protein as being related to cytochrome p450 drug-metabolizing enzyme subfamily lacks a specific asserted utility, but rather is a general asserted utility since many proteins are related to cytochrome p450 but have "completely different biological function." (see page 3 of the action).

The Examiner further states that the state of the art in protein function prediction is reviewed by Whissock et al. (*Q. Rev. Biophys.* 36(3):307-340, 2003), and represents that Whissock teaches that prediction of protein structure and function is "a difficult problem" and that prediction of function "is not a substitute for laboratory experimentation." (see page 3, last paragraph and bridging over to page 4, first paragraph).

Applicants respectfully traverse this rejection based on the following remarks.

The Applicants draw the attention of the Examiner to the third full paragraph, page 324 of Whissock et al. (*Q. Rev. Biophys., ibid)* which says "[i]n general, if an unknown protein shares a significant sequence similarity with a family of known functions, possesses the 'right essential conserved residues' (e.g. active site residues) then a prediction as to function (proteinase, exonuclease, etc.) can reasonably be proposed." Figure 2, page 1 of 3 discloses functional domains and key regions of the amino acid sequence of the invention, which include a leucine zipper, phosphorylation sites and number [7] of FIGURE 2, page 2 of 3 discloses the identity of a cytochrome p450 heme-iron ligand signature, recognized in the art as belonging to the cytochrome p450 family. Additionally, FIGURE 2, page 3 of 3 discloses that the sequence is homologous to a cytochrome p450 2G1 protein. Therefore, despite the Examiner's assertions that a 50% homology is not sufficient, one of skill in the art would *reasonably* be able to ascertain the use of the amino acid sequence given the disclosure and the state of the art. The Applicants also respectfully assert that the standard used by the Examiner, that "the claimed protein ***automatically*** has the properties and biological function of the reference protein relied on" is improper, as discussed below.

Consequently, one of skill in the art would recognize that the claimed invention does have "real world" uses, such as to act as a target to aid in prevention of cancer caused by xenobiotic carcinogens, for example. HepG-2 cells are a well-known cell line in the art for determining metabolism of various compounds, for example.

Thus, the specification does provide an enabling written description of the polypeptide of SEQ ID NO:2. Undue experimentation would not be required by one of skill in the art to use the claimed invention in light of the guidance presented, the state of the art in the area of cytochrome p450 enzymes, the skill of those in the art, and so forth (these factors are set forth in *In re Forman* and cited by the Federal Circuit in *In re Wands*).

Therefore, the claimed invention is supported by both specific and substantial utilities and, consequently, one of ordinary skill in the art would know how to use the claimed invention.

In contrast to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses

that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art, view that such molecules have uses within the commercial marketplace in the drug development cycle, becasue they encode previously unidentified members of important pharmaceutical targets, and therefore, establish the utility of the claimed invention.

The U.S. Patent and Trademark Office Utility Guidelines set forth the utility requirement that a claimed invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and in the recently adopted Utility Guidelines from the USPTO.

The Examiner stated that the present invention failed to disclose any properties of the present invention, SEQ ID NO: 2 that are associated with any disease state. However, such a requirement substantially conflicts with the decision made by the CCPA.

The CCPA in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), clearly accepted a showing of less than a specific therapeutic use of a claimed chemical compound as satisfying the utility requirement.

> *The CCPA held that where a claim does not provide evidence of pharmacological activity of a claimed compound, although it does not establish a specific therapeutic use, manifests a practical utility because knowledge of pharmacological activity is beneficial to the public in that it makes faster and easier for medical researchers to combat illnesses. Nelson v. Bowler, 206 USPQ 881 (CCPA 1980).*

The notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. Similar to the *Nelson* case, the present invention, which is drawn to isolated nucleic acid molecules that encode a cytochrome p450 (SEQ ID NO: 2), has useful value in the drug discovery process even though the molecule may not be associated with a specific treatment and/or diagnosis of a particular disease. According to *Nelson*, the present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well

recognized that cytochrome p450 are important targets for drug action. The public disclosure of a new member of this family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The amino acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the amino acid sequences of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating diseases affecting these tissues. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

The specification and figures show that the protein of the present invention has a high homology to the cytochrome p450 family. Figure 1, page 2 of 2 demonstrates a high homology with a human cytochrome p450, CYP2G. Therefore, the Applicants have provided more than a broad class of proteins; Applicants have provided the identification of a specific protein and a nucleic acid encoding said protein, and thus there is a specific and credible utility of the claimed invention. As such, there is also an enablement for one of skill in the art to make and use the invention.

Thus, the disclosure of the function of the CYP2 proteins is sufficient. Such a function is quite specific for CYP2 proteins and differentiates them from other proteins. As such, this function is specific enough to define a use for novel cytochrome p450 proteins and cytochrome p450-encoding nucleic acid molecules in the drug discovery process.

Novel cytochrome p450 proteins/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies. Thus, there is overwhelming evidence in the art to support the utility of novel cytochrome p450 proteins and encoding nucleic acid molecules. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the cytochrome p450 family of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the cytochrome p450 protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new cytochrome p450 proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present cytochrome p450 amino acid sequences. One example disclosed in the specification is that the present amino acid molecules can be used as protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely determine which biological and pathological processes the protein is involved in. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to a cytochrome p450 with a specified amino acid sequence (SEQ ID NO: 2), encoded by a specific nucleic acid sequence as SEQ ID NOS:1 and 3. Exemplary uses of the amino acid sequences are clearly recited in the specification. Among the examples, the amino acid molecules are useful as targets for identifying agents for use in therapeutic applications, drug screening assays, to identify compounds that modulate drug-metabolizing enzymes of the present invention and to screen a compound for the ability to stimulate or inhibit interaction between the drug-metabolizing enzyme protein and a molecule that normally interacts with the drug-metabolizing enzyme protein, to name a few (see the specification starting at page 19). Such uses are specific for the claimed amino acid molecules will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different amino acid molecule for the same purpose.

In view of law and fact, the Utility standard interpreted by the USPTO guidelines is too high. The disclosure of activity of the expressed polynucleotide is not required by any statute or case law interpreting the utility requirement of Section 101, and the enablement requirement of Section 112, first paragraph. The commercial value of a gene that encodes a previously unidentified member of the cytochrome p450 family, members of which are well known in the art to be commercially valuable drug targets, is sufficient to satisfy the utility and enablement requirements. Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

Rejection Under 35 U.S.C. §112, first paragraph

The Examiner rejected claims 1-9 under 35 U.S.C. §112, first paragraph because the Examiner stated that the invention "is not supported by either a specific or substantial asserted utility or a well-established utility for the reasons set forth above."

The Applicants assert that the Examiner has not met his burden of *prima facie* non-enablement or non-utility for the same reasons set forth by the applicants under 35 U.S.C. §101, *supra*.

Rejection Under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 4, 8 and 9 as being indefinite by what the Examiner states as a lack of antecedent basis for "peptide" in line 3 of claim 4. The Applicants have amended claim 4 to address the concerns of the Examiner.

Regarding the Examiner's concern that it is unclear whether claim 4 is directed to producing the polypeptide encoded by the nucleic acid of claim 1, the Applicants assert that because the limitations of an independent claim, claim 1, are incorporated into a dependent claim, claim 4, the claim unambiguously is directed to producing the polypeptide encoded by the nucleic acid of claim 1.

Claims 8 and 9 are rejected; therefore, the rejection is moot.

Applicants assert that all the concerns of the Examiner have been overcome or addressed. The Applicants respectfully request that the Examiner withdraw the rejection of the claims.

Rejection Under 35 U.S.C. §102(e)

The Examiner has rejected claims 1-4 and 7-9 under 35 U.S.C. §102(e) as being anticipated by Policky *et al.*, (WO 01/79468). The Examiner states that the priority of the '468 publication has been claimed to U.S. Provisional Application No. 60/200,185, filed on April 28, 2000. The Examiner additionally stated that "Policky et al. teach an isolated nucleic acid molecule of SEQ ID NO: 16 which encodes a protein comprising the amino acid sequence of SEQ ID NO: 2 of the instant invention."

The Applicants respectfully traverse the rejection. However, the Applicants will address the rejection to answer the concerns of the Examiner. While the Examiner provided a translation alignment of SEQ ID NO: 16 of the '185 application, she did not provide a nucleic acid to nucleic acid alignment. There is no factual evidence provided by the Examiner that ANY of the nucleic acids of the '185 application are "completely

complementary" to SEQ ID NO: 1 or SEQ ID NO: 3 as required in amended claim 1(c) of the present application, or "consist" or "comprise" SEQ ID NO: 1 or SEQ ID NO: 3 of the present application, as required in amended claim 1(a) and 1(b).

As the reference does not teach each and every limitation of the amended claim, *i.e.*, a nucleic acid of SEQ ID NO: 1, the rejection is improper and must be withdrawn.

Conclusion

Claims 1-7 and 17-21 are currently pending in the present application, with original claims 8-16 having been cancelled in the response filed September 2, 2004, as being drawn to non-elected subject matter. In view of the above remarks, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw all outstanding rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent should the Examiner believe a telephone interview would advance prosecution of the application.

Applicants respectfully assert that the claims are in condition for allowance.

Respectfully submitted,
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